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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,556	09/22/2000	Alexander Burger	016779/0154	2628

22428 7590 10/02/2003

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/667,556	BURGER ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-25,29-41 and 46-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-25,29-41 and 46-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11,18,20* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant timely responded to the PTO communication of July 16, 2002. However, due to inadvertent clerical errors, the Office has not timely responded to applicant's amendment submitted August 14, 2002. The examiner regrets any inconvenience applicant experiences due to this delay.

In the amendment submitted May 6, 2002, applicant cancelled claims 26-28, 42-45 and amended claims 16, 18, 19, 29, 35, 47 and 52-57. Also in the amendment submitted May 6, 2002, applicant added claims 58-61. In the amendment submitted August 14, 2002, applicant corrected a discrepancy within the May 6, 2002 amendment and directed the entry of claims 58-61 again. Although both sets of 58-61 are identical to each other, the Office was required to enter the claims submitted on August 14, 2002 as new claims 62-66. Therefore, claims 16-25, 29-41, 46-66 are under consideration.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

As discussed above, misnumbered claims 58-61 submitted August 14, 2002 have been renumbered 62-66.

Double Patenting

Claims 62-66 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 58-61. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-25, 29-41, 46-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 and new claims 60 and 64 require that "about 38 to about 43" amino acids of the C-terminally deleted E7 protein are deleted. This range of deletions encompassed by this limitation is indeterminate and it is not clear where the deletion is. For example, 38 to 43 amino acids could be deleted from a residue anywhere in the middle to the very last amino acid of E7. Alternatively, any 38 to 43 residues could be deleted, as long as the part of the C-terminus is deleted and it is unclear which part would be required to be deleted to retain desired function. This rejection affects all dependent claims.

Claims 23-28 and 40-57 remain vague and indefinite for reasons of record because it cannot be discerned what is intended by a "deleted" L1 or E protein. The metes and bounds of the deleted portions comprising a number of amino acids from each of the L or E proteins are

indefinite. It is suggested that applicant incorporate specific amino acid positions to be deleted into the claims found on page 7, line 27- page 8, line 12 to more clearly indicate the portions within the proteins that are to be deleted. It is again suggested that applicant incorporate specific amino acid position numbers, such as the specific examples taught, i.e., $L1\Delta CE7_{1\text{-}60}$ and $L1\Delta CE7_{1\text{-}55}$.

Applicant states that the claims have been amended to address the rejections, but the amendment does not aid in clarifying what is being claimed.

Claim 29 recites the limitation "font" in line 2. There is insufficient antecedent basis for this limitation in the claim. Applicant amended the claim to include this word, but the word has no discernable meaning within the context of the subject matter claimed.The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-25, 29-41 and 46-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 16 and new claims 60 and 64 require that "about 38 to about 43" amino acids of the C-terminally deleted E7 protein are deleted. Applicant has not pointed to support for this newly added claim limitation and the examiner is unable to locate support in the disclosure.

Applicant is required to point to support or cancel the new matter. This rejection also affects all dependent claims.

Claims 16-25, 29-41 and 46-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to deleted or C-terminally deleted L1 or E proteins, or L1 and E which have anywhere from 38-43 amino acids have been deleted in unknown portions of the proteins. The specification does not teach what structural elements of these derivations or variants encompass. The specification reduces to practice only two species within the genus, $L1\Delta CE7_{1\text{-}60}$ and $L1\Delta CE7_{1\text{-}55}$. Since the genus embraces a wide variety of possible derivatives and variants of each chimeric polypeptide or protein, the two species are not seen as representative for the full genus claimed.

Applicant asserts that the claims are drawn to a modest genus and that the specification teaches a description of a representative group of species within the genus.

Applicant's arguments and a review of the teachings of the specification have been fully considered, but are found unpersuasive.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making

the claimed product, or any combination thereof. In this case, there is not even identification of any particular portion of the proteins that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, given that the specification has only described $L1\Delta CE7_{1\text{-}60}$ and $L1\Delta CE7_{1\text{-}55}$.

Therefore, only $L1\Delta CE7_{1\text{-}60}$ and $L1\Delta CE7_{1\text{-}55}$, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 16-25, 29-41 and 46-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record.

Applicant state that the data provided in the specification and the extrinsic evidence discussed in the attached documents that the invention is fully enabling for the scope now claimed.

Applicant's arguments have been fully considered, but are found unpersuasive. The document discussed in the introduction section of the correspondence applicant refers to is presumed to be Jochmus et al. (Archives of Medical Research. 1999; 30 (4): 269-74). Jochmus et al. demonstrate that L1ΔCE7$_{1-60}$ CVPLs and VLPs have a high degree of structural resemblance, react with the papillomavirus receptor on mouse red blood cells and induce an E7-specific CTL response. Jochmus et al. also teach that 27% of mice developed tumors upon inoculation of L1ΔCE7$_{1-60,}$ while the other mice remained tumor-free for 12 weeks after tumor cell injection. This data does not indicate that the instant composition is therapeutic because almost 1/3 of the mice developed tumors and there is no data on prophylactic efficacy.

The data in the working examples also does not indicate that the chimeric fusion protein protects or treats papillomavirus infection. On page 21, lines 11 and 12, the specification states that "[v]accination with L1ΔC CVLPs did not protect against the tumour..". The *in vivo* working example include small groups of 3-5 mice that received L1ΔCE7$_{1-60}$, L1ΔCE7$_{1-55}$, L1ΔC VLP, or buffer followed by challenge with TC-1 syngeneic tumor cells. The TC-1 cells used to challenge the mice in the reference and the working example would not be realistic to natural exposure since papillomavirus infection is a result of contact with virions. For the preventative working example on page 20, line 29-page 21, line 26, the data does not suggest that the mice were protected against tumor growth since a delayed onset of tumor growth occurred. Also, the time period of two months would not be indicative of prophylactic effects of the instant composition

since papillomavirus dysplasia/carcinoma can develop years after exposure. The treatment working example on page 21, line 28-page 22, line 6, states that all of the mice that received $L1\Delta CE7_{1-60}$ remained tumor-free for two months after the tumor cell injection. There is no data that would indicate that the tumor-free period lasted for a prolonged period of time. Also, due the small number of subjects in each experiment, the results of each are inconclusive.

Applicant has supplied art regarding the sensitivity of a single amino acid change in the composition, but broadly claims that any amino acid deletion within a range of amino acids within any portion of the L1 and E proteins of any human papillomavirus will be effective in treating and preventing any form of HPV-specific tumors. However, it there is no guidance provided by the inventor on how the skilled artisan would be able to make all of the possible chimeric particles that encompass the claimed deletions, while maintaining ameliorative and prophylactic capabilities.

Therefore, the breadth of the claims encompassing a broad range of deletions within the L1 and E proteins from any papillomavirus, the lack of skill in the art for making chimeric HPV CVLPs capable of treating and preventing any HPV-tumor, the lack of guidance provided by the inventor illustrating how to make the HPV CVLPs with the desired function of treating and preventing HPV-tumors, the lack of data in the working examples demonstrating treatment or preventative characteristics of the instant composition, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make and use the invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley

JAMES HOUSEL 10/1/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600